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The relationship between physiological stress and wildlife disease: consequences for health and conservation

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Abstract

Wildlife populations are under increasing pressure from a variety of threatening processes, ranging from climate change to habitat loss, that can incite a physiological stress response. The stress response influences immune function, with potential consequences for patterns of infection and transmission of disease among and within wildlife, domesticated animals and humans. This is concerning because stress may exacerbate the impact of disease on species vulnerable to extinction, with consequences for biodiversity conservation globally. Furthermore, stress may shape the role of wildlife in the spread of emerging infectious diseases (EID) such as Hendra virus (HeV) and Ebola virus. However, we still have a limited understanding of the influence of physiological stress on infectious disease in wildlife. We highlight key reasons why an improved understanding of the relationship between stress and wildlife disease could benefit conservation, and animal and public health, and discuss approaches for future investigation. In particular, we recommend that increased attention be given to the influence of

anthropogenic stressors including climate change, habitat loss and management interventions on disease dynamics in wildlife populations.

Additional keyword: physiology.

Introduction

Stress can be broadly defined as a change in the psychological, physiological and/or physical well being of a living organism as a result of exposure to any biological and/or environmental factor that acts as a stressor (challenge to regulatory capacity). Wildlife encounter a range of stressors or threatening processes ranging from habitat loss to climate change, which may activate the hypothalamic–pituitary–adrenal (HPA) axis (stress response) (Madliger and Love 2014). The stress response is not inherently detrimental, but rather, is a complex and essential negative-feedback system involving glucocorticoids among other neuro-endocrine mediators. Thus, the HPA axis regulates the physiological, biochemical and behavioural processes required to maintain allostasis (homeostasis through change; Sapolsky *et al*. 2000; McEwen 2005). Busch and Hayward (2009) proposed a log-quadratic model for the relationship between glucocorticoids and fitness, which illustrated how the stress response (hereby referred to as 'stress') has a critical adaptive advantage up to a point, but when regulatory mechanisms are overcome, allostatic overload occurs and stress incurs fitness costs (McEwen 2005; Busch and Hayward 2009). For example, severe acute and unpredictable or chronic stressors may not allow the HPA axis to reach a recovery phase, resulting in dysfunction of the negative feedback mechanism and subsequent health impairment (Tsigos and Chrousos 1994).

In terms of infectious disease, cost of allostatic overload can include increased infection susceptibility, shedding of infectious agents, severity of clinical signs and poor prognosis (Biondi and Zannino 1997; Agarwal and Marshall 2001). As a result, shifts may occur in the host–parasite equilibrium, the healthy balance between host and parasites that have co-evolved over millennia (Aapanius 1998;

Martin 2009). Stress may affect the host–parasite equilibrium via complex interactions with, and direct influence on the immune system (Reichlin 1993; Munck and Náray-Fejes-Tóth 1994; Daynes *et al*. 1995; Sapolsky *et al*. 2000). Mediators of the HPA axis, for example, glucocorticoids, can have profound effects on different immunological processes (Sheridan *et al*. 1994; Aapanius 1998) via receptors on immune cells (Besedovsky and del Rey 1996) and changes in immune gene expression in target tissues (Padgett and Glaser 2003). Stress may also affect host–parasite equilibrium indirectly, for example, by changing characteristics of the protective mucus membranes of the body (Chester 1992) and via behavioural changes that may alter disease transmission pathways (Broom 2003). Studies in laboratory animals (Dhabhar and McEwen 1997), livestock (Salak-Johnson and McGlone 2007), fish (Maule *et al*. 1989) and humans (Biondi and Zannino 1997) have indicated that stress can affect patterns of infectious disease (Sheridan *et al*. 1994). Stress has also been suggested as a factor influencing a wide range of diseases in wildlife, including *Chlamydia* infection in koalas (Brearley *et al*. 2013), toxoplasmosis in various marsupials (Thompson *et al*. 2010), chytridimycosis in amphibians (Blaustein *et al*. 2012; Kindermann *et al*. 2012; Gabor *et al*. 2013), avian influenza in migratory birds (Weber and Stilianakis 2007) and white nose syndrome (Cryan *et al*. 2010) and zoonotic (spread from animals to humans) viruses in bats, including Ebola and Hendra virus (HeV) (Groseth *et al*. 2007; Plowright *et al*. 2014). However, associations between stress and disease in wildlife are not commonly empirically tested.

Stress has the potential to significantly alter wildlife immune function; however, the extent to which this translates into changes in patterns of infectious disease in wildlife populations remains unclear (Martin 2009; Blaustein *et al*. 2012). So as to assess this outstanding question, we evaluated the literature on physiological stress and infectious disease. We interrogated the *ISI Web of Science* (http://www.isiwebofknowledge.com, verified December 2014) by using keywords such as stress, glucocorticoids, wildlife, infection, disease, bacteria, virus, fungi, parasite and pathogen. We selected those studies that examined the influence of stress on infectious diseases in wildlife, using parallel measures of glucocorticoids and infection indices. The reference lists in these sources were also inspected to find further papers.

We concentrated on the relationship between extrinsic stressors and infectious disease in captive and free-ranging vertebrate wildlife including fish, amphibians, reptiles, birds and mammals. Previous reviews have suggested that stress can also affect immunity in other organisms across the evolutionary spectrum (Ottaviani and Franceschi 1996), including invertebrates (Adamo 2012), molluscs (Saarinen and Taskinen 2005; Hooper *et al*. 2007) and corals (Peters 1984); however, these were considered beyond the scope of the present review that concentrates on stress and disease in vertebrate wildlife. Studies focusing on domesticated fauna in agriculture or aquaculture (Cohen and Kinney 2007) were excluded because they have examined either selectively bred animals that may not react to stressors in the same way as do free-ranging wildlife, or wild-caught animals or those with limited generations in captivity. This is due to vastly different stressor exposure and genetics because the stress response is shaped by both previous exposure (Bejder *et al*. 2009) and heritable traits (Zhou *et al*. 2008).

We focussed on glucocorticoids and their metabolites as stress physiology indicators for consistency, and because glucocorticoids provide insights into the mechanisms underpinning the physiological stress response (Cooke *et al*. 2013). Glucocorticoids have been demonstrated to alter physiological, biochemical and behavioural processes to maintain allostasis during exposure to stressors (Sapolsky *et al*. 2000; McEwen 2005). They can also be measured in wildlife by using minimally invasive methods (Sheriff *et al*. 2011) and are widely acknowledged as a practical tool in conservation physiology, wildlife research and management (Cooke *et al*. 2013; Narayan 2015).

The importance of increased attention to stress and wildlife disease

As the frequency and severity of stressors increase globally, the relationship between stress and disease in wildlife populations demands greater attention (Lafferty and Kuris 1999; Aguirre and Tabor 2008; Van Bressem *et al*. 2009; Blaustein *et al*. 2012). Infection can influence animal populations via sublethal effects reducing fitness as well as dramatic population-level effects (Scott 1988; Aguirre and Tabor 2008). For example, Owen *et al*. (2012) found that experimentally elevated plasma

corticosterone can reduce the survival of northern cardinals (*Cardinalis cardinalis*) infected with West Nile virus (Owen *et al*. 2012). Similarly, Pedersen and Greives (2008) demonstrated experimentally that stress, parasitism and malnutrition drive winter population crashes in white-footed mice (*Peromyscus leucopus*). In addition, improving our understanding of the relationship between stress and the incidence, prevalence, intensity, recrudescence and severity of disease in wildlife could benefit biodiversity conservation and One Health (Zinsstag *et al*. 2011). One Health encompasses the collaborative goals of providing optimal health for people, animals (domestic and wild) and the environment, by considering interactions among these three systems (Thompson 2013).

Here, we outline the importance of increased research, monitoring and management of stress and infectious disease in wildlife populations and discuss approaches for future investigation. We draw particular attention to the following three key anthropogenic stressors that human society can practically and directly manage: climate change, habitat disturbance and management interventions.

(1) Climate change

Climate change can have a profound effect on disease dynamics in wildlife populations (Hoberg and Brooks 2015). In part, these effects may be mediated by stress because climate change involves a suite of proximate stressors such as thermal extremes and resource limitations (Geyer *et al*. 2011) that elicit a host stress response. For example, chronic stress, such as that associated with resource limitations resulting from prolonged drought, is suspected as a major risk factor for chlamydiosis in koalas, a disease that threatens population survival (Davies *et al*. 2014).

Stress linked to extreme weather events has also been suggested as a contributing factor in mass-mortality events in threatened wildlife species. For example, the normally benign bacteria *Pasteurella hamolytica*, which can be precipitated by stress, has been linked to catastrophic mass-mortality events in the critically endangered saiga antelope (*Saiga tatarica*) following severe winters (Bekenov *et al*. 1998). Recent modelling of data from over 720 animal mass-mortality events in over 2400 populations has indicated that mortality events associated with concurrent stressors and disease have increased in frequency from the 1940s to 2000s (Fey *et al*. 2015). The imperative to investigate the

relationship between stress and disease in wildlife is greater now than ever. Monitoring glucocorticoid parameters and infection indices in wildlife populations over time will allow comparisons to be made as threatening processes progress. In addition, if we can identify which host, pathogen and/or environmental factors (Fig. 1) influence animal responses to major threats such as climate change, we may be better equipped to make conservation decisions (for example, designing selection criteria for managed relocation programs).

(2) Habitat disturbance

Brearley *et al*. (2013) reviewed the profound impact that habitat loss and fragmentation can have on the prevalence of wildlife disease, and highlighted the role that stress was likely to play as a mediator of this impact. Recent studies have examined the physiological stress response of wildlife to habitat loss and fragmentation (Davies *et al*. 2013). There have also been studies linking infection patterns in wildlife to habitat loss and fragmentation (Gillespie and Chapman 2006; Hing *et al*. 2013). However, there appears to be an absence of research that unites physiology and disease diagnoses, measuring glucocorticoid and infection indices in parallel, so as to understand links among habitat loss, stress and infection patterns in wildlife.

Investigating stress and disease in wildlife can also help us identify host factors particular to individuals, populations or species that are resilient (Jessop *et al*. 2013) in an increasingly urbanised world (Fig. 1). For example, the Australian long nosed bandicoot (*Permales nasuta*) and southern brown bandicoot (*Isoodon obesulus*) had faecal glucocorticoid metabolites in the suburbs of Sydney similar to those in National Parks, and metabolites did not co-vary with ectoparasite burden, suggesting that, as generalists able to flourish in a variety of environments, these species may possess traits that make them adaptable to stress and parasite infection in a changing landscape (Dowle *et al*. 2013). The following question arises: what traits allow some individuals, populations or species to be more resilient to the synergistic effects of stress and infectious disease? Models have been developed in livestock for genetic selection and breeding for robustness based on the stress response (Mormède *et al*. 2011) and, in the future, wildlife management too may employ similar strategies to build populations that are more resilient to the combined effects of stress and disease.

Climate change and habitat loss are among the key anthropogenic stressors that are significant in terms of the One Health paradigm, which centres on inextricable links among environmental, animal and human health (Daszak *et al*. 2000; Fig. 2). These links are exemplified in modelling of global emerging infectious disease (EID) data from 1950 to 2008, which indicated a positive association between the number of threatened mammal and bird species and outbreaks of zoonoses in the Asia–Pacific region (Morand *et al*. 2014). If environmental threats trigger a stress response in wildlife that precipitates infectious disease, there may be consequences for the transmission of zoonotic EID (Fig. 2). This is particularly concerning because Jones *et al*. (2008) highlighted that over 60% of global EID are zoonoses and wildlife represent the most common source (over 70%). Hence, improving our understanding of how stress affects patterns of disease in wildlife populations will benefit One Health.

Catastrophic contemporary disease outbreaks such as Ebola virus have raised urgent questions about how environmental stressors and interactions among humans, livestock and wildlife influence the role of wildlife in disease emergence and transmission (Fenton *et al*. 2006; Myers *et al*. 2013; Plowright *et al*. 2014). However, the role of wildlife stress in EID epidemiology has yet to be elucidated. Studies have suggested that environmental stressors encountered by wildlife, including climate change and habitat loss, may precipitate zoonotic disease transmission (Hoberg and Brooks 2015). Epidemiological studies have identified trends that suggest that stress-related immunosuppression in flying foxes (pteropid bats; such as that associated with reproduction, poor nutrition, habitat loss, climate change) may have contributed to the emergence of zoonoses, including HeV and Nipah viruses, spread from flying foxes to domestic animals and humans (see the case study ‘physiological stress in bats and HeV control’ later in the paper; Plowright *et al*. 2008*a*, 2008*b*, 2011, 2014).

(3) Wildlife management interventions

An understanding of the relationship between physiological stress and disease in wildlife will help us improve the planning, design, execution and evaluation of wildlife management interventions. It is crucial that we characterise how wildlife respond to research and conservation interventions such as capture and handling (de Villiers *et al*. 1995; Narayan *et al*. 2012) and translocation (Kahn *et al*. 2007) to assess risk, minimise harm and increase the efficacy of these activities. For example, it has

been suggested that the stress of translocation is associated with increased risk of infectious disease in translocated wildlife (Teixeira *et al*. 2007; Dickens *et al*. 2010; Sainsbury and Vaughan-Higgins 2012), including recrudescence of latent and normally innocuous pathogens as well as increased vulnerability to diseases at the release site to which the translocated animals may not have been previously exposed (Mihok *et al*. 1992). However, parallel endocrine and infection investigations have rarely been conducted before, during and after wildlife translocations or, indeed, in instances of wild capture (moving of wild animals into captivity), to investigate the influence of stress and disease in translocation success and the health of translocated and resident populations. A study by Kahn *et al*. (2007) is a notable exception, finding that translocation of gopher tortoises (*Gopherus polyphemus*) did not appear to have a significant effect on corticosterone, immune parameters or infection with *Mycoplasma agassizii*, a common cause of upper respiratory disease in tortoises.

Stress and wildlife disease in management interventions also have relevance to One Health. For example, recent research has suggested that stress and disease in wildlife are highly relevant to the management of bovine tuberculosis (*Mycobacterium bovis*), which is an economically significant livestock, wildlife and zoonotic disease with ramifications for agriculture and food security (Cross *et al*. 1998; George *et al*. 2014). Stress has been linked to increased shedding of *M. bovis* in badgers (*Meles meles*) in the United Kingdom (George *et al*. 2014). These findings have direct relevance for *M. bovis* and badger management. They suggest that stressful interventions such as culling may contribute to increased shedding by wildlife hosts (Carter *et al*. 2007). Greater attention to stress and wildlife disease will help design effective wildlife policy and management plans with potential benefits to One Health, welfare, biosecurity, agriculture and associated financial consequences.

Approaches to understand the relationship between stress and disease in wildlife

There are many different ways stress and disease can be investigated in wildlife; however, here we discuss the merits and challenges of an approach using glucocorticoids and infection indices measured

in parallel. This approach has rarely been applied in wildlife, but has been recommended as a means to investigate the impact of anthropogenic activities on wild animals (Muehlenbein 2009). Combining glucocorticoid and infection indices with assessments of host reproductive history (Narayan *et al*. 2012) and survivorship (de Villiers *et al*. 1995) has also been proposed as an approach to investigate the fitness costs of stress.

Glucocorticoid indices are advantageous for investigating stress and disease in wildlife because they provide a mechanistic understanding of the underlying physiological processes mediating the stress response and are being increasingly used in wildlife research (Cooke *et al*. 2013). We now have at our disposal minimally invasive and non-invasive tools to investigate stress and disease in wildlife (Sheriff *et al*. 2011; Hunt *et al*. 2013; Narayan 2013). Using validated enzyme immunoassays and radioimmunoassays, glucocorticoids can be measured in the peripheral circulation (Palme *et al*. 2005). Alternatively, glucocorticoid metabolite concentration can be measured in faeces (Palme 2005), urine (McMichael *et al*. 2014), feathers (Bortolotti *et al*. 2008), saliva (Majchrzak *et al*. 2014), exhaled breath (Hunt *et al*. 2013) and water (Gabor *et al*. 2013). Research on glucocorticoid receptors may also prove useful to evaluate stress and disease in wildlife, although these methods remain invasive (Liebl and Martin 2013).

Parallel glucocorticoid and infection parameters have been measured in few studies; however, these studies have included species ranging from the seahorse (Anderson *et al*. 2011) to amphibians (Kindermann *et al*. 2012; Gabor *et al*. 2013), birds (Lindström *et al*. 2005; Kitaysky *et al*. 2010), lizards (Oppliger *et al*. 1998) and non-human primates (Chapman *et al*. 2006; Clough *et al*. 2010), indicating the potential of this method to be used in different taxa. This approach has been applied in a small number of stress and disease studies conducted on endangered species in challenging field conditions (Aguirre *et al*. 1995; Chapman *et al*. 2006). For example, plasma corticosterone positively correlated with fibropapilloma virus, an emerging disease threatening endangered green turtle (*Chelonia mydas*; Aguirre *et al*. 1995). Stress and infection indices were also found to correlate in endangered red colobus monkeys (*Piliocolobus badius*) where a positive correlation was observed among poor nutrition, parasitism and faecal glucocorticoid metabolites (Chapman *et al*. 2006).

There are numerous challenges, both theoretical and practical, to investigating stress and disease in wildlife by using glucocorticoids and infection parameters in parallel, particularly methodological limitations and pitfalls in the interpretation of results. First, researchers must keep in mind that the relationship between stress and infection is likely to vary depending on a variety of stressor, host, environment and pathogen factors (Fig. 1). Second, caution must be exercised when interpreting the results of glucocorticoid assays (Lane 2006; Dantzer *et al*. 2014). For example, high glucocorticoid values are not necessarily detrimental and low values beneficial, particularly if chronic stress leads to dysfunction of the HPA axis, rendering an animal unable to mount an appropriate stress response (Busch and Hayward 2009; Narayan and Hero 2014). Caution must also be exercised when interpreting changes in glucocorticoids solely as physiological responses to stressors because variations in glucocorticoids can occur normally, for example, with diurnal rhythms, exercise, pain, season and reproduction (Lane 2006).

Another challenge in the interpretation of stress and wildlife disease studies is that infection itself can act as a stressor, elevating glucocorticoids as part of the host's efforts to mobilise energy and redistribute resources towards fighting infection while also preventing collateral damage to the body (Sapolsky *et al*. 2000; Dunn 2007; Laver *et al*. 2012). For example, wild-captured rodents experimentally exposed to fleas had higher faecal glucocorticoid metabolite concentrations than did controls (St Juliana *et al*. 2014), and male fence lizards (*Sceloporus occidentalis*) naturally infected with *Plasmodium mexicanum* mounted a greater corticosterone response to capture and handling than did uninfected lizards (Dunlap and Schall 1995). The bi-directional relationship between stress and infection poses a challenge to establishing causality in observation studies. Experimental approaches can be used to investigate causality and the multi-dimensional nature of the stress–disease relationship, including experimental stressors (Oppliger *et al*. 1998), experimental infections (Warne *et al*. 2011; Kindermann *et al*. 2012; Marino *et al*. 2014) and parasite treatment experiments (Goldstein *et al*. 2005; Raouf *et al*. 2006; Pedersen and Greives 2008; Monello *et al*. 2010). However, experimental approaches have numerous logistical and ethical challenges, particularly when working with small populations of free-ranging endangered species. Captive populations may serve as useful

surrogates for experimental studies of stress and wildlife disease, provided that limitations are acknowledged, such as potential behavioural and physiological differences between captive and wild counterparts, and the stressors that may be alleviated or imposed by captivity itself (Narayan *et al*. 2012).

There are also considerations when measuring infection indices in wildlife. For example, faecal egg counts for parasite oocysts and viral titres can naturally vary with demographic, temporal and spatial variables, and potentially co-vary with the same factors that influence the stress response (Plowright *et al*. 2014). Limitations of diagnostic tests (such as detection threshold, sensitivity and specificity) must also be considered, particularly if tests are being adapted for use in wildlife species for the first time. Continuous testing and validation of sampling methods, assay protocols and experimental designs will be necessary to build robust research programs that can reliably and efficiently evaluate the relationship between stress and disease in wildlife species.

Case study: physiological stress in bats and Hendra virus (HeV) control

Improving our understanding of the relationship between physiological stress and disease dynamics in bat populations may be a key strategy to help characterise the epidemiology of HeV, predict outbreaks and protect animal and human health (Plowright *et al*. 2008*b*, 2014; McMichael *et al*. 2014). HeV, a RNA virus of the family *Paramyxoviridae* and genus *Henipavirus*, was identified as an emerging zoonotic disease in Australia in 1994 (Field *et al*. 2007). *Pteropus* species of fruit bats, including vulnerable species such as grey-headed flying fox (*Pteropus poliocephalus*), have been identified as the asymptomatic natural reservoir hosts (Young *et al*. 2000). Horses develop highly fatal respiratory or neurological disease after oronasal exposure to HeV virions in bat secretions including urine (Westbury 2000; Marsh *et al*. 2011). Following direct contact with sick horses, veterinary and stable staff have contracted severe meningoencephalitis, which, in four cases, proved fatal (Playford *et al*. 2010). Eastern-coast states of Australia continue to report sporadic equine cases (New South Wales Department of Primary Industries 2015).

The epidemiology of HeV remains incompletely understood, particularly the host and environment factors driving spill-over events (Hyatt *et al*. 2004; Smith *et al*. 2011). Changes in flying fox ecology associated with anthropogenic stressors including climate change, habitat fragmentation and urbanisation, have been proposed as drivers of HeV disease dynamics (Bradley and Altizer 2007; Plowright *et al*. 2011; Dietrich *et al*. 2015). These ultimate stressors are associated with proximate stressors such as nutritional stress, which are, in turn, overlaid on challenges such as the demands of reproduction (Plowright Field *et al*. 2008). Although experimental evidence is not available at this time, a leading hypothesis is that physiological stress alters bat immune function and increases the rate of virion shedding (Plowright *et al*. 2008*a*, 2008*b*). Hence, physiological stress may be one of the important factors influencing HeV emergence and outbreaks.

Currently McMichael *et al*. (2014) are conducting parallel investigations into glucocorticoid metabolites and HeV dynamics. This valuable information on the relationship between physiological stress in bats and HeV will inform policy and management of flying fox populations. The potential effects of stress to flying foxes on HeV spill-over has been discussed at a policy and legislative level in Australia and, on these grounds, highly disruptive methods employed overseas for 'bat control', such as culling (Florens 2012), are now banned in some Australian jurisdictions (Degeling and Kerridge 2013). However, stressful management interventions for 'problem' flying fox populations continue to be applied in Australia. For example, aversive stimuli such as noise cannons are used sporadically to drive bats away from urban centres where people complain about noise, smell and damage to gardens (Degeling and Kerridge 2013). Information about significant stressors associated with HeV virion shedding would inform cost–benefit evaluation of disruptive management approaches and would be a valuable resource on which to formulate public health advice.

Hendra virus provides a contemporary example of how the relationship between physiological stress and disease dynamics can inform responsible, evidence-based One Health and wildlife-conservation policy and management. More broadly, the above case study may have implications for other emerging viral diseases for which bats act as reservoir hosts, including Ebola (Calisher *et al*. 2006; Plowright *et al*. 2008*b*, 2014; Smith and Wang 2013).

Conclusions

Despite suggestions that stress plays an important role in disease dynamics, this remains a neglected area in wildlife research. Rhyan and Spraker (2010) described how mounting stressors may profoundly change disease-transmission cycles using the analogy of 'adding bags of sand to a rowboat until it sinks'. Understanding the dynamics of stress and disease in wildlife will help us keep healthy biological systems 'afloat' by identifying novel management targets and assisting priority setting and policy decisions.

Wider application of stress physiology and diagnostic tools to characterise links between stress and disease in wildlife will benefit One Health and biodiversity conservation. Greater collaboration between human and animal health experts, conservation researchers, comparative physiologists and disease ecologists will enable further progress in understanding the stress–disease synergism to prevent the loss of iconic species and reduce the risk of contemporary and emerging infectious diseases.

We propose a defined approach using parallel glucocorticoid parameters and infection indices to investigate stress and disease in wildlife. This approach can be applied to examine the influence of physiological stress associated with key anthropogenic stressors, including climate change, habitat disturbance and management interventions, on disease dynamics. It is time to fully incorporate stress and wildlife disease in the overall management of environmental, animal and human health.

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References

Aapanius, V. (1998). Stress and immune defense. *Advances in the Study of Behavior* **27**, 133–153.

Adamo, S. (2012). The effects of the stress response on immune function in invertebrates : an evolutionary perspective on an ancient connection. *Hormones and Behavior* **62**, 324–330.

Agarwal, S. K., and Marshall, G. D. (2001). Stress effects on immunity and its application to clinical immunology. *Clinical and Experimental Allergy* **31**, 25–31.

Aguirre, A. A., and Tabor, G. M. (2008). Global factors driving emerging infectious diseases. *Annals of the New York Academy of Sciences* **1149**, 1–3.

Aguirre, A. A., Balazs, G. H., Spraker, T. R., and Gross, T. S. (1995). Adrenal and hematological responses to stress in juvenile green turtles (*Chelonia mydas*) with and without fibropapillomas. *Physiological Zoology* **68**, 831–854.

Anderson, P. a., Berzins, I. K., Fogarty, F., Hamlin, H. J., and Guillette, L. J. (2011). Sound, stress, and seahorses: the consequences of a noisy environment to animal health. *Aquaculture* **311**, 129–138.

Bejder, L., Samuels, A., Whitehead, H., Finn, H., and Allen, S. (2009). Impact assessment research: use and misuse of habituation, sensitisation and tolerance in describing wildlife responses to anthropogenic stimuli. *Marine Ecology Progress Series* **395**, 177–185.

Bekenov, A. B., Grachev, I. A., and Milner-Gulland, E. J. (1998). The ecology and management of the saiga antelope in Kazakhstan. *Mammal Review* **28**, 1–52.

Besedovsky, H. O., and del Rey, A. (1996). Immune-neuro-endocrine interactions: facts and hypotheses. *Endocrine Reviews* **17**, 64–102.

Biondi, M., and Zannino, L.-G. (1997). Psychological stress, neuroimmunomodulation, and susceptibility to infectious diseases in animals and man: a review. *Psychotherapy and Psychosomatics* **66**, 3–26.

Blaustein, A. R., Gervasi, S. S., Johnson, P. T. J., Hoverman, J. T., Belden, L. K., Bradley, P. W., and Xie, G. Y. (2012). Ecophysiology meets conservation: understanding the role of disease in amphibian population declines. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* **367**, 1688–1707.

Bortolotti, G. R., Marchant, T. A., Blas, J., and German, T. (2008). Corticosterone in feathers is a long-term, integrated measure of avian stress physiology. *Functional Ecology* **22**, 494–500.

Bradley, C. A., and Altizer, S. (2007). Urbanization and the ecology of wildlife diseases. *Trends in Ecology & Evolution* **22**, 95–102.

Brearley, G., Rhodes, J., Bradley, A., Baxter, G., Seabrook, L., Lunney, D., Liu, Y., and McAlpine, C. (2013). Wildlife disease prevalence in human-modified landscapes. *Biological Reviews of the Cambridge Philosophical Society* **88**, 427–442.

Broom, D. M. (2003). Transport stress in cattle and sheep with details of physiological, ethological and other indicators. *Deutsche Tierarztliche Wochenschrift* **110**, 83–89.

Busch, D. S., and Hayward, L. S. (2009). Stress in a conservation context: a discussion of glucocorticoid actions and how levels change with conservation-relevant variables. *Biological Conservation* **142**, 2844–2853.

Calisher, C. H., Childs, J. E., Field, H. E., Holmes, K. V., and Schountz, T. (2006). Bats: important reservoir hosts of emerging viruses. *Clinical Microbiology Reviews* **19**, 531–545.

Carter, S. P., Delahay, R. J., Smith, G. C., Macdonald, D. W., Riordan, P., Etherington, T. R., Pimley, E. R., Walker, N. J., and Cheeseman, C. L. (2007). Culling-induced social perturbation in Eurasian badgers *Meles meles* and the management of TB in cattle: an analysis of a critical problem in applied ecology. *Proceedings of the Royal Society of London. Series B, Biological Sciences* **274**, 2769–2777.

Chapman, C. A., Wasserman, M. D., Gillespie, T. R., Speirs, M. L., Lawes, M. J., Saj, T. L., and Ziegler, T. E. (2006). Do food availability, parasitism, and stress have synergistic effects on red colobus populations living in forest fragments? *American Journal of Physical Anthropology* **131**, 525–534.

Chester, A. C. (1992). Psychological stress and the common cold. *The New England Journal of Medicine* **326**, 645–646.

Clough, D., Heistermann, M., and Kappeler, P. M. (2010). Host intrinsic determinants and potential consequences of parasite infection in free-ranging red-fronted lemurs (*Eulemur fulvus rufus*). *American Journal of Physical Anthropology* **142**, 441–452.

Cohen, N., and Kinney, K. (2007). Exploring the phylogenetic history of neural-immune system interactions: an update. In 'Psychoneuroimmunology'. (Ed. R. Ader.) pp. 1–38. (Elsevier: Burlington, MA.)

Cooke, S. J., Sack, L., Franklin, C. E., Farrell, A. P., Beardall, J., Wikelski, M., and Chown, S. L. (2013). What is conservation physiology? Perspectives on an increasingly integrated and essential science. *Conservation Physiology* **1**, cot001.

Cross, M. L., Swale, E., Young, G., and Mackintosh, C. (1998). Effect of field capture on the measurement of cellular immune responses in wild ferrets (*Mustela furo*), vectors of bovine tuberculosis in New Zealand. *Veterinary Research* **30**, 401–410.

Cryan, P. M., Meteyer, C. U., Boyles, J. G., and Blehert, D. S. (2010). Wing pathology of white-nose syndrome in bats suggests life-threatening disruption of physiology. *BMC Biology* **8**, 135.

Dantzer, B., Fletcher, Q. E., Boonstra, R., and Sheriff, M. J. (2014). Measures of physiological stress: a transparent or opaque window into the status, management and conservation of species? *Conservation Physiology* **2**, cou023.

Daszak, P., Cunningham, A. A., and Hyatt, A. D. (2000). Emerging infectious diseases of wildlife: threats to biodiversity and human health. *Science* **287**, 443–449.

Davies, N. A., Gramotnev, G., McAlpine, C., Seabrook, L., Baxter, G., Lunney, D., Rhodes, J. R., and Bradley, A. (2013). Physiological stress in koala populations near the arid edge of their distribution. *PLoS One* **8**, e79136.

Davies, N., Gramotnev, G., Seabrook, L., McAlpine, C., Baxter, G., Lunney, D., and Bradley, A. (2014). Climate-driven changes in diet composition and physiological stress in an arboreal folivore at the semi-arid edge of its distribution. *Biological Conservation* **172**, 80–88.

Daynes, R. A., Araneo, B. A., Hennebold, J., Enioutina, E., and Mu, H. H. (1995). Steroids as regulators of the mammalian immune response. *The Journal of Investigative Dermatology* **105**, 14S–19S.

Degeling, C., and Kerridge, I. (2013). Hendra in the news: public policy meets public morality in times of zoonotic uncertainty. *Social Science & Medicine* **82**, 156–163.

Dhabhar, F. S., and McEwen, B. S. (1997). Acute stress enhances while chronic stress suppresses cell-mediated immunity *in vivo*: a potential role for leukocyte trafficking. *Brain, Behavior, and Immunity* **11**, 286–306.

Dickens, M. J., Delehanty, D. J., and Michael Romero, L. (2010). Stress: an inevitable component of animal translocation. *Biological Conservation* **143**, 1329–1341.

Dietrich, M., Wilkinson, D. A., Benlali, A., Lagadec, E., Ramasindrazana, B., Dellagi, K., and Tortosa, P. (2015). *Leptospira* and paramyxovirus infection dynamics in a bat maternity enlightens pathogen maintenance in wildlife. *Environmental Microbiology* **17**, 4280–4289.

Dowle, M., Webster, K. N., and Deane, E. (2013). Faecal glucocorticoid metabolite concentrations in the free-ranging bandicoots (*Perameles nasuta* and *Isoodon obesulus*) of northern Sydney. *Australian Mammalogy* **35**, 1–7.

Dunlap, K. D., and Schall, J. J. (1995). Hormonal alterations and reproductive inhibition in male fence lizards (*Sceloporus occidentalis*) Infected with the malarial parasite *Plasmodium mexicanum*. *Physiological Zoology* **68**, 608–621.

Dunn, A. J. (2007). Infection as a stressor: a cytokine-mediated activation of the hypothalamo–pituitary–adrenal axis? In 'Ciba Foundation Symposium 172. Corticotropin-releasing Factor'. (Ed. K. Ackrill.) pp. 226–242. (John Wiley & Sons: Chichester, UK) Available at

Fenton, M., Davison, M., Kunz, T., McCracken, G., Racey, P., Tuttle, M., and Dobson, A. (2006). Linking bats to emerging diseases. *Science* **311**, 1098c–1099c.

Fey, S. B., Siepielski, A. M., Nusslé, S., Cervantes-Yoshida, K., Hwan, J. L., Huber, E. R., Fey, M. J., Catenazzi, A., and Carlson, S. M. (2015). Recent shifts in the occurrence, cause, and magnitude of animal mass mortality events. *Proceedings of the National Academy of Sciences, USA* **112**, 1083–1088.

Field, H. E., Mackenzie, P. J. S., and Daszak, P. (2007). Henipaviruses: emerging paramyxoviruses associated with fruit bats. In 'Wildlife and Emerging Zoonotic Diseases: the Biology, Circumstances and Consequences of Cross-species Transmission. Current Topics in Microbiology and Immunology'. (Eds J. E. Childs, J. S. Mackenzie and J. A. Richt.) pp. 133–159. (Springer Berlin: Heidelberg, Germany.)

Florens, F. B. V. (2012). Going to bat for an endangered species. *Science* **336**, 1102.

Gabor, C. R., Fisher, M. C., and Bosch, J. (2013). A non-invasive stress assay shows that tadpole populations infected with *Batrachochytrium dendrobatidis* have elevated corticosterone levels. *PLoS One* **8**, e56054.

George, S., Smith, T., Cana, P., Coleman, R., and Montgomery, W. (2014). Physiological stress in the Eurasian badger (*Meles meles*): effects of host, disease and environment. *General and Comparative Endocrinology* **200**, 54–60.

Geyer, J., Kiefer, I., Kreft, S., Chavez, V., Salafsky, N., Jeltsch, F., and Ibisch, P. L. (2011). Classification of climate-change-induced stresses on biological diversity. *Conservation Biology* **25**, 708–715.

Gillespie, T. R., and Chapman, C. A. (2006). Prediction of parasite infection dynamics in primate metapopulations based on attributes of forest fragmentation. *Conservation Biology* **20**, 441–448.

Goldstein, E. J., Millspaugh, J. J., Washburn, B. E., Brundige, G. C., and Raedeke, K. J. (2005). Relationships among fecal lungworm loads, fecal glucocorticoid metabolites, and lamb recruitment in free-ranging Rocky Mountain bighorn sheep. *Journal of Wildlife Diseases* **41**, 416–425.

Groseth, A., Feldmann, H., and Strong, J. E. (2007). The ecology of Ebola virus. *Trends in Microbiology* **15**, 408–416.

Hing, S., Othman, N., Nathan, S. K. S. S., Fox, M., Fisher, M., and Goossens, B. (2013). First parasitological survey of endangered Bornean elephants *Elephas maximus borneensis*. *Endangered Species Research* **21**, 223–230.

Hoberg, E. P., and Brooks, D. R. (2015). Evolution in action: climate change, biodiversity dynamics and emerging infectious disease. *Philosophical Transactions of the Royal Society of London B: Biological Sciences* **370**, 20130553.

Hooper, C., Day, R., Slocombe, R., Handlinger, J., and Benkendorff, K. (2007). Stress and immune responses in abalone: limitations in current knowledge and investigative methods based on other models. *Fish & Shellfish Immunology* **22**, 363–379.

Hunt, K. E., Moore, M. J., Rolland, R. M., Kellar, N. M., Hall, A. J., Kershaw, J., Raverty, S. A., Davis, C. E., Yeates, L. C., Fauquier, D. A., Rowles, T. K., and Kraus, S. D. (2013). Overcoming the challenges of studying conservation physiology in large whales: a review of available methods. *Conservation Physiology* **1**, cot006.

Hyatt, A. D., Daszak, P., Cunningham, A. A., Field, H., and Gould, A. R. (2004). Henipaviruses: gaps in the knowledge of emergence. *EcoHealth* **1**, 25–38.

Jessop, T. S., Woodford, R., and Symonds, M. R. E. (2013). Macrostress: do large-scale ecological patterns exist in the glucocorticoid stress response of vertebrates? Ed R. Boonstra. *Functional Ecology* **27**, 120–130.

Jones, K. E., Patel, N. G., Levy, M. A., Storeygard, A., Balk, D., Gittleman, J. L., and Daszak, P. (2008). Global trends in emerging infectious diseases. *Nature* **451**, 990–993.

Kahn, P. F., Guyer, C., and Mendonça, M. T. (2007). Handling, blood sampling and tempory captivity do not affect plasma corticosterone or movement patterns of gopher tortoises (*Gopherus polyphemus*). *Copeia* **2007**, 614–621.

Kindermann, C., Narayan, E. J., and Hero, J.-M. (2012). Urinary corticosterone metabolites and chytridiomycosis disease prevalence in a free-living population of male Stony Creek frogs (*Litoria wilcoxii*). *Comparative Biochemistry and Physiology. Part A, Molecular & Integrative Physiology* **162**, 171–176.

Kitaysky, A. S., Piatt, J. F., Hatch, S. A., Kitaiskaia, E. V., Benowitz-Fredericks, Z. M., Shultz, M. T., and Wingfield, J. C. (2010). Food availability and population processes: severity of nutritional stress during reproduction predicts survival of long-lived seabirds. *Functional Ecology* **24**, 625–637.

Lafferty, K. D., and Kuris, A. M. (1999). How environmental stress affects the impacts of parasites. *Limnology and Oceanography* **44**, 925–931.

Lane, J. (2006). Can non-invasive glucocorticoid measures be used as reliable indicators of stress in animals? *Animal Welfare* **15**, 331–342.

Laver, P. N., Ganswindt, A., Ganswindt, S. B., and Alexander, K. A. (2012). Non-invasive monitoring of glucocorticoid metabolites in banded mongooses (*Mungos mungo*) in response to physiological and biological challenges. *General and Comparative Endocrinology* **179**, 178–183.

Liebl, A. L., and Martin, L. B. (2013). Stress hormone receptors change as range expansion progresses in house sparrows. *Biology Letters* **9**, 20130181.

Lindström, K. M., Hawley, D. M., Davis, A. K., and Wikelski, M. (2005). Stress responses and disease in three wintering house finch (*Carpodacus mexicanus*) populations along a latitudinal gradient. *General and Comparative Endocrinology* **143**, 231–239.

Madliger, C. L., and Love, O. P. (2014). The need for a predictive, context-dependent approach to the application of stress hormones in conservation. *Conservation Biology* **28**, 283–287.

Majchrzak, Y. N., Mastromonaco, G. F., Korver, W., and Burness, G. (2014). Use of salivary cortisol to evaluate the influence of rides in dromedary camels. *General and Comparative Endocrinology* , .

Marino, J. A., Holland, M. P., and Maher, J. (2014). Predators and trematode parasites jointly affect larval anuran functional traits and corticosterone levels. *Oikos* **123**, 451–460.

Marsh, G. A., Haining, J., Hancock, T. J., Robinson, R., Foord, A. J., Barr, J. A., Riddell, S., Heine, H. G., White, J. R., Crameri, G., Field, H. E., Wang, L.-F., and Middleton, D. (2011). Experimental infection of horses with Hendra virus/Australia/horse/2008/Redlands. *Emerging Infectious Diseases* **17**, 2232–2238.

Martin, L. B. (2009). Stress and immunity in wild vertebrates: timing is everything. *General and Comparative Endocrinology* **163**, 70–76.

Maule, A. G., Tripp, R. A., Kaattari, S. L., and Schreck, C. B. (1989). Stress alters immune function and disease resistance in chinook salmon (*Oncorhynchus tshawytscha*). *The Journal of Endocrinology* **120**, 135–142.

McEwen, B. S. (2005). Stressed or stressed out: what is the difference? *Journal of Psychiatry & Neuroscience* **30**, 315–318.

McMichael, L., Edson, D., and Field, H. (2014). Measuring physiological stress in Australian flying-fox populations. *EcoHealth* **11**, 400–408.

Mihok, S., Olubayo, R. O., and Moloo, S. K. (1992). Trypanosomiasis in the black rhinoceros (*Diceros bicornis* Linnaeus, 1758). *Revue Scientifique et Technique* **11**, 1169–1173.

Monello, R. J., Millspaugh, J. J., Woods, R. J., and Gompper, M. E. (2010). The influence of parasites on faecal glucocorticoid metabolite levels in raccoons: an experimental assessment in a natural setting. *Journal of Zoology* **282**, 100–108.

Morand, S., Jittapalapong, S., Suputtamongkol, Y., Abdullah, M. T., and Huan, T. B. (2014). Infectious diseases and their outbreaks in Asia-Pacific: biodiversity and its regulation loss matter. *PLoS One* **9**, e90032.

Mormède, P., Foury, A., Terenina, E., and Knap, P. W. (2011). Breeding for robustness: the role of cortisol. *Animal: An International Journal of Animal Bioscience* **5**, 651–657.

Muehlenbein, M. (2009). The application of endocrine measures in primate parasite ecology. In 'Primate Parasite Ecology: the Dynamics and Study of Host–parasite Relationships'. (Eds A. Huffman and C. Chapman.) pp. 63–81. (Cambridge University Press, Cambridge, UK) Available at http://www.indiana.edu/~ecolab/pubs/Muehlenbein_2009_Chapter.pdf [Verified 20 January 2015]

Munck, A., and Náray-Fejes-Tóth, A. (1994). Glucocorticoids and stress: permissive and suppressive actions. *Annals of the New York Academy of Sciences* **746**, 115–130, discussion 131–133.

Myers, S. S., Gaffikin, L., Golden, C. D., Ostfeld, R. S. H., Redford, K. H., Ricketts, T., Turner, W. R., and Osofsky, S. A. (2013). Human health impacts of ecosystem alteration. *Proceedings of the National Academy of Sciences, USA* **110**, 18753–18760.

Narayan, E. (2013). Non-invasive reproductive and stress endocrinology in amphibian conservation physiology. *Conservation Physiology* **1**, cot011.

Narayan, E. J., and Hero, J.-M. (2014). Repeated thermal stressor causes chronic elevation of baseline corticosterone and suppresses the physiological endocrine sensitivity to acute stressor in the cane toad (*Rhinella marina*). *Journal of Thermal Biology* **41**, 72–76.

Narayan, E., Hero, J., Evans, N., Nicolson, V., and Muccib, A. (2012). Non-invasive evaluation of physiological stress hormone responses in a captive population of the greater bilby *Macrotis lagotis*. *Endangered Species Research* **18**, 279–289.

Narayan, E. J. (2015). Evaluation of physiological stress in Australian wildlife: embracing pioneering and current knowledge as a guide to future research directions. *General and Comparative Endocrinology* , .

New South Wales Department of Primary Industries (2015). Hendra virus confirmed near Lismore 4 September 2015. Available at http://www.dpi.nsw.gov.au/aboutus/news/all/2015/hendra-virus-confirmed-near-lismore [Verified 11 December 2015]

Oppliger, A., Clobert, J., Lecomte, J., and Boudjemadi, K. (1998). Environmental stress increases the prevalence and intensity of blood parasite infection in the common lizard *Lacerta vivipara*. *Ecology Letters* **1**, 129–138.

Ottaviani, E., and Franceschi, C. (1996). The neuroimmunology of stress from invertebrates to man. *Progress in Neurobiology* **48**, 421–440.

Owen, J. C., Nakamura, A., Coon, C. A., and Martin, L. B. (2012). The effect of exogenous corticosterone on West Nile virus infection in northern cardinals (*Cardinalis cardinalis*). *Veterinary Research* **43**, 34.

Padgett, D. A., and Glaser, R. (2003). How stress influences the immune response. *Trends in Immunology* **24**, 444–448.

Palme, R. (2005). Measuring fecal steroids: guidelines for practical application. *Annals of the New York Academy of Sciences* **1046**, 75–80.

Palme, R., Rettenbacher, S., Touma, C., and El-Bahr, S. M. (2005). Stress hormones in mammals and birds: comparative aspects regarding metabolism, excretion, and noninvasive measurement in fecal samples. *Annals of the New York Academy of Sciences* **1040**, 162–171.

Pedersen, A. B., and Greives, T. J. (2008). The interaction of parasites and resources cause crashes in a wild mouse population. *Journal of Animal Ecology* **77**, 370–377.

Peters, E. (1984). A survey of cellular reactions to environment stress and disease in Caribbean scleractinian corals. *Helgoländer Meeresuntersuchungen* **37**, 113–137.

Playford, E. G., McCall, B., Smith, G., Slinko, V., Allen, G., Smith, I., Moore, F., Taylor, C., Kung, Y.-H., and Field, H. (2010). Human Hendra virus encephalitis associated with equine outbreak, Australia, 2008. *Emerging Infectious Diseases* **16**, 219–223.

Plowright, R. K., Field, H. E., Smith, C., Divljan, A., Palmer, C., Tabor, G., Daszak, P., and Foley, J. E. (2008*a*). Reproduction and nutritional stress are risk factors for Hendra virus infection in little red flying foxes (*Pteropus scapulatus*). *Proceedings. Biological Sciences* **275**, 861–869.

Plowright, R. K., Sokolow, S. H., Gorman, M. E., Daszak, P., and Foley, J. E. (2008*b*). Causal inference in disease ecology: investigating ecological drivers of disease emergence. *Frontiers in Ecology and the Environment* **6**, 420–429.

Plowright, R. K., Foley, P., Field, H. E., Dobson, A. P., Foley, J. E., Eby, P., and Daszak, P. (2011). Urban habituation, ecological connectivity and epidemic dampening: the emergence of Hendra virus from flying foxes (*Pteropus* spp.). *Proceedings of the Royal Society of London. Series B, Biological Sciences* **278**, 3703–3712.

Plowright, R. K., Eby, P., Hudson, P. J., Smith, I. L., Westcott, D., Bryden, W. L., Middleton, D., Reid, P. A., McFarlane, R. A., Martin, G., Tabor, G. M., Skerratt, L. F., Anderson, D. L., Crameri, G., Quammen, D., Jordan, D., Freeman, P., Wang, L.-F., Epstein, J. H., Marsh, G. A., Kung, N. Y., and McCallum, H. (2014). Ecological dynamics of emerging bat virus spillover. *Proceedings of the Royal Society of London. Series B, Biological Sciences* **282**, 20142124.

Raouf, S. A., Smith, L. C., Brown, M. B., Wingfield, J. C., and Brown, C. R. (2006). Glucocorticoid hormone levels increase with group size and parasite load in cliff swallows. *Animal Behaviour* **71**, 39–48.

Reichlin, S. (1993). Neuroendocrine–immune interactions. *The New England Journal of Medicine* **329**, 1246–1253.

Rhyan, J. C., and Spraker, T. R. (2010). Emergence of diseases from wildlife reservoirs. *Veterinary Pathology* **47**, 34–39.

Saarinen, M., and Taskinen, J. (2005). Long-lasting effect of stress on susceptibility of a freshwater clam to copepod parasitism. *Parasitology* **130**, 523–529.

Sainsbury, A. W., and Vaughan-Higgins, R. J. (2012). Analyzing disease risks associated with translocations. *Conservation Biology* **26**, 442–452.

Salak-Johnson, J. L., and McGlone, J. J. (2007). Making sense of apparently conflicting data: stress and immunity in swine and cattle. *Journal of Animal Science* **85**, E81–E88.

Sapolsky, R. M., Romero, L. M., and Munck, A. U. (2000). How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocrine Reviews* **21**, 55–89.

Scott, M. E. (1988). The impact of infection and disease on animal populations: implications for conservation biology. *Conservation Biology* **2**, 40–56.

Sheridan, J. F., Dobbs, C., Brown, D., and Zwilling, B. (1994). Psychoneuroimmunology: stress effects on pathogenesis and immunity during infection. *Clinical Microbiology Reviews* **7**, 200–212.

Sheriff, M. J., Dantzer, B., Delehanty, B., Palme, R., and Boonstra, R. (2011). Measuring stress in wildlife: techniques for quantifying glucocorticoids. *Oecologia* **166**, 869–887.

Smith, I., and Wang, L.-F. (2013). Bats and their virome: an important source of emerging viruses capable of infecting humans. *Current Opinion in Virology* **3**, 84–91.

Smith, I., Broos, A., de Jong, C., Zeddeman, A., Smith, C., Smith, G., Moore, F., Barr, J., Crameri, G., Marsh, G., Tachedjian, M., Yu, M., Kung, Y. H., Wang, L.-F., and Field, H. (2011). Identifying Hendra virus diversity in pteropid bats. *PLoS One* **6**, e25275.

St Juliana, J. R., Khokhlova, I. S., Wielebnowski, N., Kotler, B. P., and Krasnov, B. R. (2014). Ectoparasitism and stress hormones: strategy of host exploitation, common host–parasite history and energetics matter. *Journal of Animal Ecology* , .

Teixeira, C. P., De Azevedo, C. S., Mendl, M., Cipreste, C. F., and Young, R. J. (2007). Revisiting translocation and reintroduction programmes: the importance of considering stress. *Animal Behaviour* **73**, 1–13.

Thompson, R. C. A., Lymbery, A. J., and Smith, A. (2010). Parasites, emerging disease and wildlife conservation. *International Journal for Parasitology* **40**, 1163–1170.

Thompson, R. C. A. (2013). Parasite zoonoses and wildlife: one health, spillover and human activity. *International Journal for Parasitology* **43**, 1079–1088.

Tsigos, C., and Chrousos, G. (1994). Physiology of the hypothalamic–pituitary–adrenal axis in health and dysregulation in psychiatric and autoimmune disorders. *Endocrinology and Metabolism Clinics of North America* **23**, 451–466.

Van Bressem, M.-F., Raga, J. A., Di Guardo, G., Jepson, P. D., Duignan, P. J., Siebert, U., Barrett, T., Santos, M. C. de O., Moreno, I. B., Siciliano, S., Aguilar, A., and Van Waerebeek, K. (2009). Emerging infectious diseases in cetaceans worldwide and the possible role of environmental stressors. *Diseases of Aquatic Organisms* **86**, 143–157.

Villiers, M. S., Meltzer, D. G. A., Heerden, J. V., Mills, M. G. L., Richardson, P. R. K., and Jaarsveld, A. S. V. (1995). Handling-induced stress and mortalities in African wild dogs (*Lycaon pictus*). *Proceedings of the Royal Society of London. Series B, Biological Sciences* **262**, 215–220.

Warne, R., Crespi, E., and Brunner, J. (2011). Escape from the pond: stress and developmental responses to ranavirus infection in wood frog tadpoles. *Functional Ecology* **25**, 139–146.

Weber, T. P., and Stilianakis, N. I. (2007). Ecologic immunology of avian influenza (H5N1) in migratory birds. *Emerging Infectious Diseases* **13**, 1139–1143.

Westbury, H. (2000). Hendra virus disease in horses. *Revue Scientifique et Technique* **19**, 151–159.

Young, P. L., Halpin, K., Mackenzie, J. S., and Field, H. E. (2000). Isolation of Hendra virus from pteropid bats: a natural reservoir of Hendra virus. *Journal of General Virology* **81**, 1927–1932.

Zhou, Z., Zhu, G., Hariri, A. R., Enoch, M.-A., Scott, D., Sinha, R., Virkkunen, M., Mash, D. C., Lipsky, R. H., Hu, X.-Z., Hodgkinson, C. A., Xu, K., Buzas, B., Yuan, Q., Shen, P.-H., Ferrell, R. E., Manuck, S. B., Brown, S. M., Hauger, R. L., Stohler, C. S., Zubieta, J.-K., and Goldman, D. (2008). Genetic variation in human NPY expression affects stress response and emotion. *Nature* **452**, 997–1001.

Zinsstag, J., Schelling, E., Waltner-Toews, D., and Tanner, M. (2011). From 'One Medicine' to 'One Health' and systemic approaches to health and well-being. *Preventive Veterinary Medicine* **101**, 148–156.

Fig. 1. Factors that may influence the response of wildlife to stress and disease. Stress, host, parasite and environment factors may influence the response of wildlife to stress and disease.

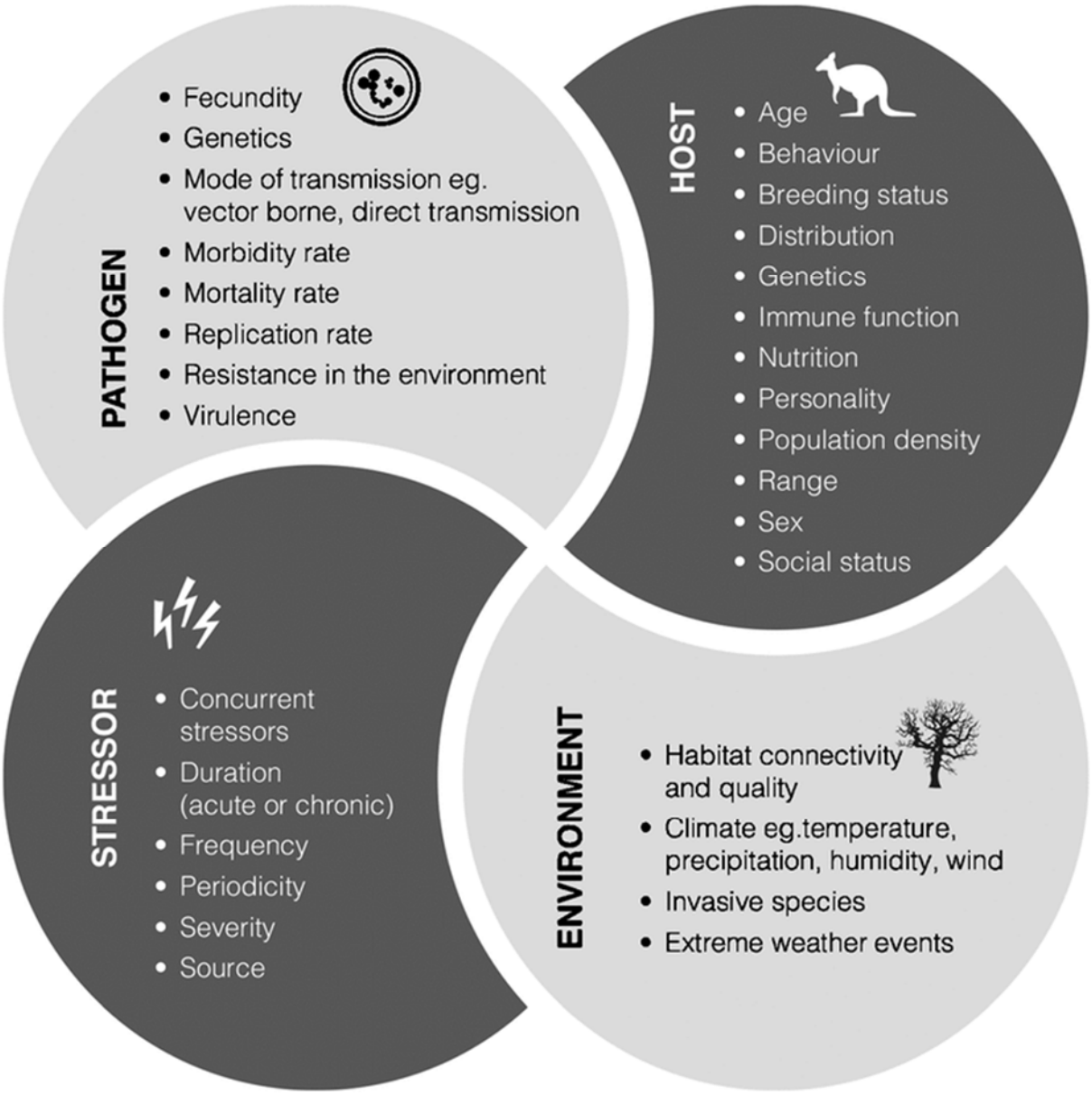

Fig. 2. Stress and disease in One Health. Conceptual flow diagram of how the physiological relationship between stress and disease may shape the role of wildlife in the transmission of emerging infectious disease. (1) Stress to wildlife can influence infection dynamics and wildlife may also be a source of stress. (2) The environment can be a source of stress and stress can also influence the hosts' interaction with the environment. (3) Pathogens can act as a stress and stress can also affect infection dynamics. (4) Environmental factors may influence the stress and disease response of wildlife and wildlife may also contribute to environmental change. (5) Pathogens may be shed into the environment and environmental factors can facilitate persistence of pathogens. (6) Humans can be a source of environmental stress and environmental factors can also influence human infection dynamics. (7) Pathogens may affect the whole wildlife host stress response and stress may exacerbate infection. (8) Some pathogens can infect humans, domestic hosts and wildlife. (9) Interactions among humans, domestic hosts and wildlife can facilitate disease transmission. (10) Humans and domestic animals may be a source of stress for wildlife but may also be susceptible to many of the same stressors. The heavier dashed lines and related bolded text represent priority interactions and/or influences.